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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,043	12/16/2004	Shinya Nagashima	Q85356	7583

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2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
03/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,043	NAGASHIMA ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,7,9,10 and 13-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,3,4,6,7,9,10 and 15-25* is/are allowed.

6)☒ Claim(s) *13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20071220*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on December 20, 2007.

Claims 1, 3-4, 6-7, 9-10 and 13-25 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

1. Claims 13-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the treatment of asthma or COPD, does not reasonably provide enablement for a method for inhibiting STAT 6 activation in a subject; or a method for inhibiting Th2 cell differentiation induced by STAT6 activation in a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. The instant claims 13-14 continue to be in 'reach-through' format. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions, for which they lack written description and enabling disclosure in the specification. Further, there is no

disclosure regarding how the subject suffering from a condition which, for example, requires the biological activity of 'inhibition of STAT6 activation or inhibition of Th2 cell differentiation induced by STAT6 activation' and further, how the appropriate therapeutic effect is generally produced in the subject. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art.

As clearly explained in the previous office action, the instant claims encompass treatment of all types of respiratory and allergic diseases which can affect different organs causing diverse vulnerabilities. The development of the most efficacious strategy for the treatment of the claimed diseases is based on understanding the underlying mechanisms of each type of disease. Some of the diseases encompassed by the instant claims involve a multi-step, multi-mechanism process and many of the types of the diseases of the instant claims are not alike, in spite of some apparent universal characteristics. Therefore, it is maintained that applicants have not provided sufficient test assays or data to support the instantly claimed treatment or other activity commensurate in scope with the claims, as of the filing date of the application.

Applicant argues that 'the specification describes testing assays which are related to measuring STAT6-dependent reporter or Th2 differentiation activity' and further, argues that 'the specification shows tests of STAT6 inhibitors in the COPD-related animal model'. The instant claims, however, encompass treatment of allergic, inflammatory respiratory diseases, etc. and there is nothing in the specification or the state of the art which establishes the therapeutic activity of the instant compounds based on the biological activity.

Applicant cites state of the art references to provide support for the therapeutic activity of the instant claims. However, the submitted state of the art references do not establish the

therapeutic activity encompassed by the instant claims. See, for example, Kuperman et al., provides that: "It is not yet clear which of the many pathways that contribute to asthma pathogenesis are good therapeutic targets. The airway epithelium and its cell-surface IL-13 receptors are readily accessible to inhaled drugs. Our results suggest that blocking these receptors, or the downstream signaling pathways activated by their ligation, could provide one strategy to improve the specificity of asthma treatment" (see page 887). The reference is clearly indicative of the uncertainty of the biological activity related to airway or respiratory diseases. The references at most provides at best establish activity related to the treatment of asthma and COPD. The references clearly illustrate the unpredictability of biological pathways and mechanisms associated with the recited STAT6 activity and therefore, one skilled in the art would not reach the conclusion whether or not the compound will be effective in treating all types of allergic diseases, respiratory diseases, etc., without going through undue experimentation.

When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

Applicant has not provided sufficient evidence that establishes that the disclosure would have enabled for one skilled in the art at the time of filing. Further, the state of the art does not identify a single class of compounds that can treat all types of diseases or possess the biological activity of the instant claims. Further, one skilled in the art of medicinal therapy recognizes that there are complex interactions between individual genetic, developmental state, sex, dietary,

environmental, drug, and lifestyle factors that contribute to the carcinogenic process, making it even more challenging to have a single therapeutic agent for the treatment of diverse diseases. Rigorously planned and executed clinical trials, incorporating measurement of appropriate biomarkers and pharmacodynamic endpoints are critical for selecting the optimal dose and schedule. A detailed understanding of the molecular mode of action, alongside the elucidation of the molecular pathology of individual diseases is required to identify disease types and individual patients that may benefit most from treatment. It is also important to construct a pharmacologic audit trail linking molecular biomarkers and pharmacokinetic and pharmacodynamic parameters to receptor response endpoints. Therefore, it is maintained that applicants have not provided sufficient test assays or data to support the various methods commensurate in scope with the claims, as of the filing date of the application.

2. Claims 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Hisamichi et al., WO 99/31073 (cited in IDS). (U.S. Patent No. 6,432,963 which belongs to the same patent family, also cited in IDS, is reviewed as the WO publication is not in English). The reference teaches substituted pyrimdine compounds, see the compounds of Examples 8 and 52 of Table 5. The reference teaches that the compounds are useful as pharmaceutical therapeutic agents. The instant claims recite 'a method for inhibitory activity of STAT 6 activation in a subject' and 'a method for inhibitory activity for Th2 cell differentiation in a subject' using a compound of formula (I) and the specification provides that the compounds are useful in the treatment of respiratory diseases such as asthma, see page 45. The reference compounds are also disclosed to be useful as pharmaceutical therapeutic agents for the treatment of asthma, etc., see col. 13, lines

20-38. The reference and the instant claims recite administration of the compounds to the same patient population in same dosages for the same therapeutic utility.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that 'the claims are drawn to a method of inhibiting STAT6 and Th2 cell differentiation and the reference does not teach or suggest these methods'. The instant claims, however, are directed to administering the compound to a subject for inhibiting STAT6 or Th2 cell differentiation, and the specification provides that the activity relates to the treatment of allergic diseases, respiratory diseases, etc. Therefore, the reference and the instant claims recite administration of the compounds to the same patient population in same dosages for the same therapeutic utility.

Allowable Subject Matter

Claims 1, 3-4, 6-7, 9-10 and 15-25 are allowed. The references of record do not teach or fairly suggest the instantly claimed compounds.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

March 5, 2008